Integration of HIV Care for Women Into OBGYN Services
Objectives

- Discuss the role of the OBGYN in identification of HIV+ women
- Review obstetric and gynecologic issues in HIV infection
- Discuss potential models for integration of care
Identification of HIV
AIDS Cases among Female Adults and Adolescents Attributed to Injection Drug Use or High-Risk Heterosexual Contact, by Region, 2003–2007—50 States and DC

- **Injection drug use**: N=13,080
- **High-risk heterosexual contact**: N=35,024

**Region**
- Northeast: 4,873 (in thousands)
- Midwest: 1,207
- South: 19,091
- West: 2,900

Note: Data have been adjusted for reporting delays and missing risk-factor information.
* Heterosexual contact with a person known to have, or to be at high risk for, HIV infection.
Estimated Numbers of AIDS Cases, Deaths, and Persons Living with AIDS, 1985–2007—United States and Dependent Areas

Note. Data have been adjusted for reporting delays.
The Continuing HIV/AIDS Epidemic in the U.S.

It is estimated that >50% of new infections are accounted for by tx from individuals who do not know they have HIV (Marks et al. AIDS 2006; 20:1447)

- New Infections, 2006: ~56,000
- People Living with HIV/AIDS: ~1,100,000
- People with HIV/AIDS Not in Care: ~42-59%
- People with HIV Who Don’t Know They Are Infected: ~21%

NOTE: Data are estimates.
Late HIV diagnosis is associated with lower perceived risk, marginalized groups, and those not routinely offered testing (JAIDS 2007; 46 (suppl 1):S3)

Heterosexual transmission is associated with lower perceived risk by women and their providers

Survey (n=582) of practice patterns re: HIV testing by ACOG Fellows (Obstet Gynecol 2007;1109):

- Would strongly recommend HIV testing to non-pregnant women with:
  - Unprotected sex with multiple partners- 85.9%
  - Current STI- 72.5%
  - Planning pregnancy- 35%
  - Sexually active and not previously tested- 34.2%

- 79% of Fellows report that lack of perceived risk is a very common reason a patient declines HIV testing

- Diagnosis at more advanced stage is associated with poorer outcomes
Among 4,127 persons with AIDS*, 45% were first diagnosed HIV-positive within 12 months of AIDS diagnosis (“late testers”) (MMWR 2003)

Average survival approx 11 yrs longer when treatment is started with CD4 320/mm³ vs 87/mm³ (Moore et al. 15th CROI 2008)

Maryland: delayed dx with late entry into care has cost est. loss of 2700 life years (CID 2007;45:1369)

Extrapolating to US: approx 100,000 life-yrs lost because of late presentation (JAMA 2008;300:945)
### Time of Maternal HIV Testing among Children with Perinatally Acquired AIDS, HIV Exposure or HIV Infection Reported in 2006—United States and Dependent Areas

<table>
<thead>
<tr>
<th>Time of maternal HIV test</th>
<th>Perinatally Acquired AIDS (N=74)</th>
<th>HIV Exposure* (N=1,883)</th>
<th>HIV Infection† (N=447)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
<td>No.</td>
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<tr>
<td>Before or at birth</td>
<td>28</td>
<td>38</td>
<td>1,746</td>
</tr>
<tr>
<td>After birth</td>
<td>28</td>
<td>38</td>
<td>65</td>
</tr>
<tr>
<td>Unknown</td>
<td>18</td>
<td>24</td>
<td>72</td>
</tr>
</tbody>
</table>

*From 33 areas that report perinatal exposure.
†From 50 areas with confidential name-based HIV infection reporting.
Revised Recommendations
Pregnant Women – CDC (MMWR 2006 (RR 14), ACOG (Committee Opinion Sept 2008)

- Universal opt-out HIV screening
  - Include HIV in routine panel of prenatal screening tests
  - Consent for prenatal care includes HIV testing
- Second test in 3rd trimester for pregnant women:
  - Known to be at risk for HIV (includes incident STI in pregnancy)
  - In jurisdictions with elevated HIV incidence
  - In high HIV prevalence health care facilities (>1/1000 pregnancies)
- Opt-out rapid testing with option to decline for women with undocumented HIV status in L&D
  - Initiate ARV prophylaxis on basis of rapid test result
Revised Recommendations
Adults and Adolescents – CDC (MMWR 2006;RR-14)

- Routine, voluntary HIV screening for all persons 13-64 in health care settings, not based on risk
- Repeat HIV screening of persons with known risk at least annually
- Opt-out HIV screening with the opportunity to ask questions and the option to decline
- Include HIV consent with general consent for care; separate signed informed consent not recommended
- Document refusal in medical record
- Screen as part of routine gyn care (ACOG Committee Opinion # 411 Aug 2008)
Obstetric and Gynecologic Issues in HIV Infection
HIV providers’ lack of comfort with reproductive issues and gynecologic exam

Gynecologic issues’ actual or perceived lower level of severity compared to other medical problems

Significant discrepancy between visit compliance to primary HIV care (55%) and HIV gynecologic care (36.2%) in co-located clinics (n=1086)*

Race, substance abuse, CD4<200 are predictors of low visit compliance in gyn clinic*

*Tello, J Women’s Health 2008 ;17:1609
Frequent Gynecologic Problems in Women with HIV

- 46.9% of 262 HIV-infected women had at least one gyn condition when followed for one year (Minkoff AJOG 1999)
- 83% of women in an inpatient AIDS service had coexisting gyn disease, although only 9% were admitted with a primary gyn problem (Frankel Clin Infect Dis 1997)
- Commonly seen gyn problems
  - Menstrual disorders
  - Genital ulcer disease
  - Abnormal vaginal discharge
  - Pelvic inflammatory disease
  - HPV, cervical and other lower genital tract dysplasia, neoplasia
Gynecologic Problems and HIV

- HIV may affect incidence, presentation, natural history, or response to treatment (e.g., HSV, HPV/dysplasia)
- Expanded differential diagnoses, especially with significant immunosuppression (e.g., CMV as etiology of genital ulcers)
- Confounding variables (e.g., menstrual disorders)
- Potential increased risk of HIV acquisition or transmission with genital tract infections
Women with HIV Infection and Lower Genital Tract Neoplasia

- HIV-infected women have
  - Higher prevalence, incidence and longer persistence of HPV
  - Higher HPV viral loads
  - Higher likelihood of multiple HPV subtypes
  - Greater prevalence of oncogenic subtypes
- Abnormal cervical cytology/histology more common among HIV+ women and is associated with HPV
  - Frequency and severity of abnormal pap smears and documented dysplasia increase with declining CD4 counts and higher HIV-RNA levels
- Recent study of >2,400 HIV+ women found that almost 1 in 4 did not receive an annual Pap test (Oster et al. JAIDS 2009;51:430-436)
- Dysplasia more likely to involve other sites in lower genital tract: careful exam of vagina, vulva and perianal region recommended
Recommendations for Cervical Cytology Screening for Women with HIV Infection

- After initial HIV diagnosis, perform two Pap smears 6 months apart
- If both initial Paps are within normal limits, repeat on annual basis
- Perform colposcopy with directed biopsies with Pap smear showing ASCUS, SIL or squamous cell carcinoma
  - Data insufficient to support use of HPV DNA testing for triage of ASCUS in HIV+ women (MMWR 2009;58: No. RR-4)
- Perform colposcopy with endocervical sampling for AGC/AIS; endometrial sampling should be done in women >35 yr.
- ASCCP guidelines should be followed when CIN is identified and for further evaluation of AGC/AIS
ARV Therapy and Cervical Dysplasia/HPV

- Data mixed re: effect of ARV on HPV prevalence/persistence, incidence/regression/progression of dysplasia
- Recommendations for evaluation and follow-up are unchanged in women on HAART
HPV-related Disease and Response to HAART

- Less-advanced immunosuppression and early stages of intraepithelial neoplasia (IN) may best respond to HAART due to restoration of HPV-specific immune responses
- Poorer response to HAART with IN 2-3
  - Inability to restore HPV specific immunity or
  - Accumulation of genetic mutations so that restoration of HPV immunity insufficient to cause lesion regression
HPV-related Disease Outside the Cervix

- **HERS prospective cohort:** 192 HIV+/88 HIV-
  - Baseline 1.6% HIV+ vs 0 HIV- had vulvar, vaginal or perianal intraepithelial neoplasia
  - During f/u: 8.5% HIV+ vs 1.1% HIV- developed VIN, VAIN, PAIN; incidence 1.96/100 py HIV+ vs 0.26/100 py HIV- (p=.03)
- **WIHS prospective cohort:** 1562 HIV+/469 HIV-
  - Incid genital warts 5.01/100 py HIV+ vs 1.31/100 py HIV- (p<.001)
WIHS: 470 HIV+, 185 HIV-
- HIV+ more likely to have abn. anal cytology/histology (31% vs 9%, p<.001); abn. cervical cytology/histology (34% vs 19%, p=.003), and anal and cervical HPV (p<.001)
- No diff in hx anal sex HIV+ vs HIV-
- Among HIV+ women incidence of invasive anal cancer is 7-28X greater than in general population (J Natl Ca Inst 2000, Br J Ca 2003)
Estimated Number of Perinatally Acquired AIDS Cases by Year of Diagnosis, 1985–2006—United States and Dependent Areas

- ACTG 076 & USPHS ZDV Recs
- CDC HIV Testing Recs
- ~95% reduction

Note. Data have been adjusted for reporting delays and cases without risk factor information were proportionally redistributed.

Estimated number of births to women living with HIV infection, 2000-2006

2006 estimate (8,650 – 8900) is ~30% > 2000 estimate (6075 – 6422)

Office of Inspector General (Fleming), 2002
Whitmore, et al. CROI, 2009
Live Births Among HIV+ Women Before and After HAART Availability

- WIHS
  - Women in HAART era were younger, with higher CD4 cell counts
  - In HAART era, 150% increase in live birth rate among HIV+ women versus 5% increase among HIV- women
    - Live birth rate higher in all age categories with largest difference (306%) seen in women >35 years
    - Among HIV+ women with more than high school education, live birth rate was approximately half that of HIV- women in pre-HAART era but more than double the HIV- rate in HAART era
    - Birth rate higher in HAART era within each category of CD4 cell count
    - Women with history of intravenous drug use were the only group in both HIV+ and HIV- women who experienced a decline in birth rates

CD = cluster of differentiation.
Cumulative Incidence of First Pregnancy in 174 Perinatally HIV-Infected Sexually Active Girls Age >13 Years, PACTG 219C


By age 19 years, 24.2% of sexually active girls had been pregnant at least once (6 had 2\textsuperscript{nd} pregnancy, 1 had 3\textsuperscript{rd})

Screen for pregnancy in HIV-infected Adolescents!
Effective Contraceptive Methods are Underused in HIV Care Settings and Unwanted Pregnancy is Common

- **WIHS: (1994-2005), n=2784; 26,832 visits** (J Women’s Health 2007, 16:857)
  - Barrier methods: 30.5-36.3% of visits
  - Tubal ligation: 21.-26.5%
  - Hormonal method: <10% of visits
  - No contraception: >30%
  - HIV+ less likely to use hormonal method

- **Italy: 334 women on ART at time of conception**—57.6% unplanned pregnancies (Floridia M et al. *Antivir Ther* 2006;11:941-946)

- **HIV+ pregnant US adolescents** ($n = 1090$): HIV status known prior to pregnancy in 50%; 83.3% of pregnancies unplanned—43% of these resulted from lack of contraception (Koenig LJ et al. *Am J Obstet Gynecol*. 2007;197(3 suppl):S123-S131)
Goals of Preconception Care

- Prevention of unintended pregnancy
- Protection of maternal and fetal health during pregnancy
- Prevention of mother-to-child transmission of HIV
- Reduce risk of transmission to uninfected partner
When to Discuss Pregnancy

- Initial evaluation: assess childbearing plans/desires
- Early in course of care
  - desire for future pregnancy or uncertain
  - nonuse/inadequate use of contraception
- At intervals during routine care, especially:
  - interest in conceiving
  - nonuse/inadequate use of contraception
  - change in relationship
  - medications with potential reproductive toxicity
  - new developments in pregnancy and HIV
  - at risk for unintended pregnancy
  - enrollment in clinical trials
- Refer for preconception counseling and care!
Preconception Care

- **Interventions**
  - Contraception to reduce unintended pregnancy
  - Counseling
  - Treat anemia
  - Clinical staging/CD4 count
  - Treat OIs, if present, or begin OI prophylaxis when indicated
  - Initiate/modify ART, if indicated
    - Avoid efavirenz (EFV)
    - Ensure tolerability/lack of toxicity
    - Monitor improvement clinically/CD4
  - Screen/stop/substitute for other potential teratogens (e.g., alcohol, statins, ACE inhibitors, warfarin, lithium, carbamazepine, megestrol, phenytoin, TCN, valproic acid, and vitamin A)
  - Address other medical/psychosocial issues
WHO Medical Eligibility Criteria for Contraceptive Use

- Category 1
  - Use method in any clinical circumstances
- Category 2
  - With clinical judgment, generally use method
  - With limited clinical judgment, use method
- Category 3
  - With clinical judgment, use of method not generally recommended unless more appropriate methods not available or acceptable
  - With limited clinical judgment, do not use method
- Category 4
  - Do not use method

WHO = World Health Organization.
<table>
<thead>
<tr>
<th></th>
<th>COC/P/R</th>
<th>CIC</th>
<th>POP</th>
<th>DMPA</th>
<th>LNG-impl</th>
<th>Cu-IUD</th>
<th>LNG-IUD</th>
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<td>2</td>
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<tr>
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<td>3</td>
<td>2</td>
<td>3</td>
<td>1</td>
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CIC = combined injectable contraceptives; COC/P/R = low-dose combined oral contraceptives/patch/ring; Cu-IUD = copper intrauterine devices; LNG-impl = levonorgestrel implants; LNG-IUD = levonorgestrel-releasing intrauterine devices; POC = progestogen-only pills.

Spermicides

- Possible increase in mucosal irritation and genital ulcers, especially with frequent use

- UNAIDS clinical trial in Africa and Thailand found significantly higher HIV seroconversion rates in nonoxynol-9 users

- WHO: “high risk of HIV”: category 4

- WHO: “HIV-infected” or “AIDS”: category 3

UNAIDS = Joint United Nations Programme on HIV/AIDS.
World Health Organization: Medical Eligibility Criteria for Contraceptive Use 2008 Update
Contraceptive Methods and HIV: IUD

- **Efficacy:** 0.2–0.8/100 women at 12 months
  - 599 postpartum HIV+ women in Zambia randomized to Cu-IUD vs hormonal contraception (followed up for at least 2 years)\(^1\)
    - Pregnancy more likely in hormonal contraceptive group (HR 2.4; 95% CI, 1.3–4.7)

- **Safety**
  - No increase in cervical HIV shedding (measured 4 months after IUD insertion)\(^2\)
  - No evidence of increased complications (including infections) for HIV+ women; complications similar by CD4 cell counts\(^3,4\)
  - LNG-IUD: Significant reduction in menstrual blood loss and increase in hemoglobin and ferritin levels; serum E2 levels remained in follicular range; genital HIV shedding was not affected; levels of LNG similar with and without HAART (\(n = 12\))\(^1\)

Hormonal Contraception

- High efficacy rates
- Alternate routes of delivery and duration of action
  - Injectable (DMPA) (3 mo)
  - Implant (3 yr)
  - Transdermal patch (1 wk)
  - Vaginal ring (3 wk)
  - Intrauterine system (5 yr)
- Noncontraceptive benefits of hormonal methods
  - Decrease iron deficiency anemia
  - Decrease risk of pelvic inflammatory disease
  - Decrease incidence of endometrial, ovarian and colorectal cancer
- Drug interactions with ART
## Interactions: PIs and Hormonal Contraception

<table>
<thead>
<tr>
<th>ARV</th>
<th>Effect on EE/NE</th>
<th>Recommendation</th>
</tr>
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<td>Atazanavir</td>
<td>↑ EE 48% ↑ NE 110%</td>
<td>Alternative methods or use back up</td>
</tr>
<tr>
<td>Darunavir/ rtv</td>
<td>↓ EE</td>
<td>Alternative methods or use back up</td>
</tr>
<tr>
<td>Fos-amprenavir</td>
<td>↑ EE levels APV 20%</td>
<td>Do not co-administer</td>
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<tr>
<td>Indinavir</td>
<td>↑ EE 24% ↑ NE 26%</td>
<td>No change</td>
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<tr>
<td>Lopinavir</td>
<td>↓ EE 42%</td>
<td>Alternative methods or use back up</td>
</tr>
<tr>
<td>Nelfinavir</td>
<td>↓ EE 47% ↓ NE 18%</td>
<td>Alternative methods or use back up</td>
</tr>
<tr>
<td>Ritonavir</td>
<td>↓ EE 40%</td>
<td>Alternative methods or use back up</td>
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<tr>
<td>Saquinavir</td>
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<td>No data</td>
</tr>
<tr>
<td>Tipranavir</td>
<td>↓ EE 50%</td>
<td>Alternative methods or use back up</td>
</tr>
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## Interactions: NNRTI and Hormonal Contraception

<table>
<thead>
<tr>
<th>ARV</th>
<th>Effect on EE</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nevirapine</td>
<td>↓ EE 20%</td>
<td>Alternative methods or use back up</td>
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<tr>
<td>Efavirenz</td>
<td>↑ EE 37%</td>
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</tr>
<tr>
<td>Etravirine</td>
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<td>Dose unchanged</td>
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<tr>
<td></td>
<td>No change NE</td>
<td></td>
</tr>
</tbody>
</table>

Safety of Hormonal Contraception: Adverse Effects

- **Combined estrogen/progestin contraceptives**
  - Minor adverse effects: nausea, breast tenderness, bloating, headache—usually self-limited
  - Contraindications (estrogen/progestin)
    - History of thromboembolic disease
    - >35 years of age, smoker
    - Hypertension
    - Diabetes mellitus: age >35 years or <35 years with associated vascular disease
    - Coronary artery disease/congestive heart failure/cerebrovascular disease
    - Migraines: age >35 years or <35 years with focal neurologic signs
    - Uncontrolled low-density lipoprotein cholesterol >160 mg/dL, triglycerides >250 mg/dL, or multiple other risk factors for coronary artery disease
    - Active liver disease

- **Progestin-only contraceptives**
  - Decreased bone density with DMPA (5%–7%); significant gains in bone mass after discontinuation
  - Irregular bleeding

PMTCT: What Works?

- Maximal suppression of viral load
- Use of antiretroviral agents
  - More complex regimens more effective
  - Longer regimens more effective
  - Intrapartum and neonatal treatment important
    - Continue HAART during labor
    - IV ZDV in labor and for 6 wks to infant
- C-section when viral load not suppressed and/or on no ART or ZDV only
- Prevention and treatment of STIs
- Avoid breastfeeding
Importance of prevention of HIV acquisition during pregnancy

- Analysis of 2144 HIV+ women giving birth in NY: only 1.4% were seroconversions, but these accounted for 23.4% of all MTCT 2002-2004
- CDC analysis of 10 states: 1.4% seroconversion rate among 4006 HIV+ pregnancies; MTCT rate 29.3% vs 4.8%

Rakai, Uganda (Gray et al. Lancet 2005;366:1182)

- 2188 HIV- women with pregnancy or BF exposure and 8473 HIV- women without pregnancy/BF
- HIV incidence highest in pregnancy, despite significantly fewer external sex partners
Models of Care

Integration of OBGYN services into HIV care programs at same site
- Collaborative
- Dedicated clinicians
- Requires additional resources
- May improve follow-up
  - HCSUS: 81% women had a Pap test in last 12 months; women with a gynecologist and PCP at same site were twice as likely to have a Pap (Stein 2001)
  - Johns Hopkins AIDS service: only 48% of women had Pap within one yr of enrollment in clinic; 87% cumulative probability within 6 yr (40% Paps abnormal)
Models of Care

- Coordination of OBGYN services at different site
  - OBGYN with HIV interest and expertise
  - Delineation of referral indications
  - Formal linkages and bilateral communication
Role of HIV Provider in OBGYN Care

- Review of sexual activity and contraception and condom use at each visit
- Interval menstrual history
- Addressing childbearing plans/desires at intervals throughout care
- Early diagnosis of pregnancy
  - Missed menses or irregular bleeding
  - New onset pelvic pain
- Referrals, as indicated
Other considerations

- Peer counselors
- Continuity of care
  - OB care to postpartum gyn care
- Transition-adolescent to adult care
- Other linkages: pediatrics, substance abuse treatment
- Childcare
- Access to clinical trials
Competing issues and priorities for HIV+ women

- Women as caregivers: children or other family members with HIV take priority; childcare
- Economic dependence
- Low status of women
- Depression
- Domestic violence
  - Two-thirds of HIV+ and high-risk women had history of domestic violence; 1/4 to 1/3 had history of childhood sexual abuse (AJPH 2000;90:560)
  - 20.5% HIV+ women reported physical harm since HIV diagnosis (AJPH 2000;90:447)
- Stigma and bias of providers